small hydrophobic integral membrane protein (SH), the
hemagglutinin-neuraminidase (HN), and the polymerase protein (L)
(FIG. 3B).

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DEPR:
Using cDNAs which encode the functional anti-HER2 sFv (Batra et al.,
1992; Chen et al. 1997) and the SV5 F protein (Paterson et al.,
1984), two chimeric genes are constructed such that the extracellular
antigen binding sites of the sFv are linked precisely to portions of
the SV5 F protein (FIG. 3A). Briefly, the HER2-specific sFv consists
of the variable region of the light chain of monoclonal antibody e23
attached through a short linker segment to the variable region of the
heavy chain (Batra et al., 1992). This polypeptide has been shown to
bind with very high affinity to cell surface HER2. Using
PCR.RTM.-based methods (Parks, 1994), the sFv-F1 hybrid gene is
constructed such that the sFv polypeptide is linked precisely with
the F protein membrane spanning and cytoplasmic domains (FIG. 3A).
For the purposes of this example, two hybrid genes are constructed,
sFv-F1 and sFv-F2. The sFv-F2 hybrid gene differs from sFv-F1 by
containing an additional polypeptide segment from the F protein
extracellular domain. In turn, these two DNA fragments are engineered
such that the final cDNA is flanked by the SV5 HN gene start and gene
end sequences (Parks et al., 1992).

DEPR:
The following example is a description of the use of recombinant SV5
(rSV5) as a targeted vector to direct infection specifically to HER2
positive cells. In the following studies, two human carcinoma cell
lines are employed which express dramatically different levels of
HER2. N87 cells are a human gastric carcinoma cell line which
overexpresses cell surface HER2, and the anti-HER2 sFv shows very
strong binding to these cells (Batra et al., 1992). A characteristic
of the N87 cells which is important for preliminary studies is that
they can be used to evaluate human tumor growth in a nude mouse model
(Chen et al., 1997). The human mammary tumor cell line MCF expresses
very low to undetectable levels of HER2, and the anti-HER2 sFv shows
only background low level of binding to these cells (Chen et al.,
1997). This cell line is predicted to be resistant to infection by
rSV5-sFv-F. Other HER2-positive and -negative cell lines are also
available (e.g., SKOV3, NIH/3T3).

ORPL:
Paterson, et al, "Fusion protein of the paramyxovirus simian virus 5:
Nucleotide sequence of mRNA predicts a highly hydrophobic
glycoprotein," Proc. Natl. Acad. Sci. USA, Nov. 1984, pp. 6706-6710.

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